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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,901	11/14/2001	Michael M. Neff	SALKINS.024DV1	7032

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/992,901	NEFF ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-13,15,17-23,25 and 27-32* is/are rejected.

7)☒ Claim(s) *5,6,14,16,24 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/01;12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-32, drawn to a method of producing a genetically modified plant comprising contacting a plant cell with a vector containing an exogenous nucleic acid sequence comprising at least one structural gene encoding a BAS1 polypeptide, in the response filed March 18, 2004 is acknowledged. The traversal is on the ground(s) that a search of both Groups I and II would not be unduly burdensome. This is not found persuasive because a search of Group II requires an additional search for regulatory sequences that modify expression of an endogenous bas1 gene.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

Initialed and dated copies of Applicant's IDS forms 1449, filed November 14, 2001 and December 23, 2002, are attached to the instant Office action.

Claim Objections

Claim 12 is objected to because of the following informalities: claim 12 recites a sequence directed to a nonelected invention (a regulatory sequence that modifies expression of an endogenous *bas1* gene). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7-13, 15, 17-23, 25 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of producing a genetically modified plant characterized as having dwarf adult stature, including a genetically modified plant that exhibits green foliage that is darker than a wild-type plant, said method comprising: (a) contacting a plant cell with a vector containing an exogenous nucleic acid sequence comprising at least one structural gene of unspecified structure encoding a BASI polypeptide obtained from any unspecified source, including a sequence that has the nucleotide sequence of SEQ ID NO:1 and a BAS 1 polypeptide that has the amino acid sequence of SEQ ID NO:2, said gene being operably associated with a regulatory sequence that causes overexpression of the gene, to obtain a transformed plant cell; (b) producing a plant from said transformed plant cell; and selecting a plant exhibiting said dwarf adult stature. The claims are also drawn to a genetically modified plant.

The specification describes the *Arabidopsis thaliana bas1* nucleotide sequence as SEQ ID NO:1 (Figure 1A), which encodes the *Arabidopsis thaliana* BAS1 amino acid sequence of SEQ ID NO:2 (Figure 1B). The specification also describes SEQ ID NO:2 as a cytochrome P450 (CYP72B1) that is a C-26 hydroxylase of brassinolide, targeting brassinolide for inactivation

(page 5 lines 21-27). The specification additionally describes a BAS1 polypeptide as meaning other homologous plant cytochrome P450s, such as CYP72A from *Catharanthus roseus*, which is known in the prior art and is disclosed as having about 42% amino acid sequence identity with SEQ ID NO:2, and the CYP72 *chibi2* from *Arabidopsis,* which does not appear in the prior art and whose sequence and % identity with SEQ ID NO:2 are not disclosed (page 11 lines 20-24). The specification further describes transgenic *Arabidopsis* and tobacco plants transformed with SEQ ID NO:1 as having dwarf adult stature and exhibiting green foliage that is darker than a wild-type plant (pages 62-68). The specification does not describe other structural genes encoding other BAS1 polypeptides that are obtained from sources other than *Arabidopsis* or *Catharanthus roseus*, or plants transformed therewith.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus of sequences comprising at least one structural gene encoding a BAS1 polypeptide, nor the structural features unique to the genus.

Claims 1-4, 7-13, 15, 17-23, 25 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a

genetically modified plant characterized as having dwarf adult stature, including a genetically modified plant that exhibits green foliage that is darker than a wild-type plant, by transforming a plant with an exogenous nucleic acid sequence encoding a BAS 1 polypeptide having the amino acid sequence of SEQ ID NO:2, does not reasonably provide enablement for methods of transforming plants with other exogenous nucleic acid sequences of unspecified sequence encoding other BAS 1 polypeptides obtained from unspecified sources. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of producing a genetically modified plant characterized as having dwarf adult stature, including a genetically modified plant that exhibits green foliage that is darker than a wild-type plant, said method comprising: (a) contacting a plant cell with a vector containing an exogenous nucleic acid sequence comprising at least one structural gene of unspecified structure encoding a BASI polypeptide obtained from any unspecified source, including a sequence that has the nucleotide sequence of SEQ ID NO:1 and a BAS 1 polypeptide that has the amino acid sequence of SEQ ID NO:2, said gene being operably associated with a regulatory sequence that causes overexpression of the gene, to obtain a transformed plant cell; (b) producing a plant from said transformed plant cell; and selecting a plant exhibiting said dwarf adult stature. The claims are also drawn to a genetically modified plant.

The specification discloses the cloning of an *Arabidopsis thaliana bas1* nucleotide sequence which encodes the *Arabidopsis thaliana* BAS1 amino acid sequence of SEQ ID NO:2 (pages 61-68). The specification also discloses that SEQ ID NO:2 is a cytochrome P450

(CYP72B1) that is a C-26 hydroxylase of brassinolide, targeting brassinolide for inactivation (page 5 lines 21-27). The specification additionally discloses that a BAS1 polypeptide includes other homologous plant cytochrome P450s, such as CYP72A from *Catharanthus roseus*, which is known in the prior art and is disclosed as having about 42% amino acid sequence identity with SEQ ID NO:2, and the CYP72 *chibi2* from *Arabidopsis,* which does not appear in the prior art and whose sequence and % identity with SEQ ID NO:2 are not disclosed (page 11 lines 20-24). The specification further discloses transgenic *Arabidopsis* and tobacco plants transformed with SEQ ID NO:1 as having dwarf adult stature and exhibiting green foliage that is darker than a wild-type plant (pages 62-68). The specification does not disclose other structural genes encoding other BAS1 polypeptides that are obtained from sources other than *Arabidopsis* or *Catharanthus roseus*, or plants transformed therewith.

The full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance with respect to where and how to obtain exogenous nucleic acid sequences encoding BAS1 polypeptides obtained from sources other than *Arabidopsis* or *Catharanthus roseus* plants. Such guidance is necessary because one cannot predictably obtained BAS1 polypeptides from other sources. The specification discloses that the *Arabidopsis thaliana* BAS1 amino acid sequence of SEQ ID NO:2 codes for a cytochrome P450 protein, which proteins are known to exhibit diversity with respect to their specific functions in plants, such that a BAS1 polypeptide could not be predictably selected on the basis of its identity as a cytochrome P450 protein alone.

See for example Mizutani et al. (Plant Molecular Biology, Vol. 37, pages 39-52, 1998), who teach that cytochrome P450s are involved in the oxidative metabolism of diverse

endogenous and exogenous lipophilic substrates, and play crucial roles in the biosynthesis of compounds such as fatty acids, sterols, phenylpropanoids, terpenoids, phytoalexins and gibberellins, as well as in the detoxification of herbicides, in plants (page 39 columns 1 and 2). Mizutani et al. also teach that studies of plant cytochrome P450s have been impeded by their instability and low abundance, and further teach that it has been difficult to elucidate physiological functions for cloned sequences encoding plant cytochrome P450s (page 39 column 2 through page 40 column 1 first paragraph).

Given the diverse specific functions exhibited by different cytochrome P450s in plants, it would require undue experimentation for one skilled in the art to identify and clone from undisclosed sources sequences encoding polypeptides having homology to the *Arabidopsis* BAS1 polypeptide of SEQ ID NO:2, as one skilled in the art would have to test by trial and error the effect of expressing each homologous sequence he or she obtains on the phenotype of a plant transformed therewith.

Given the claim breadth which encompasses the use of any structural gene of unspecified structure encoding a BASI polypeptide obtained from any unspecified source whose expression in a plant transformed therewith would result in dwarf adult stature and green foliage that is darker than a wild-type plant, given the unpredictability in obtaining BASI polypeptides from other sources as discussed above, and given the lack of guidance as discussed above, it would have required undue experimentation for one skilled in the art to make and use the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-13, 15, 17-18, 21-23, 25, 27-29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Mangold et al. (Plant Science, Vol. 96, pages 129-136, 1994).

The claims are drawn to a genetically modified dicotyledonous plant comprising at least one exogenous sequence encoding a BAS1 polypeptide in its genome and further containing multiple exogenous nucleic acid sequences encoding a BAS1 polypeptide, wherein the plant is characterized as having dwarf adult stature, wherein the plant comprises darker green leaves in adult plants, and wherein the exogenous nucleic acid sequence is operably associated with a regulatory sequence comprising a constitutive promoter. The claims are also drawn to a seed that germinates into a plant comprising at least one exogenous bas1 nucleic acid sequence in its genome.

Mangold et al. teach the cloning of a sequence encoding a cytochrome P450 (CYP72 family) obtained from *Catharanthus roseus*, and genetically modified dicotyledonous tobacco and *Arabidopsis* plants comprising said sequence, wherein the sequence is operably associated with a regulatory sequence comprising a constitutive 35S CaMV promoter (page 129 Abstract, page 133 Figure 2).

While Mangold et al. do not explicitly teach an exogenous nucleic acid sequence encoding a cytochrome P450 (CYP72 family) obtained from *Catharanthus roseus* is a "BAS1"

polypeptide, the sequence used by Mangold et al. is necessarily a "BAS1" polypeptide, since Applicant's specification indicates at page 11 lines 20-24 that the term "BAS1 polypeptide" as used herein means other plant cytochrome p450s homologous to SEQ ID NO:2 such as the CYP72A from *Catharanthus roseus* used by Mangold et al. While Mangold et al. do not explicitly teach that their genetically modified plants further contain multiple exogenous nucleic acid sequences encoding a BAS1 polypeptide, the genetically modified plants taught by Mangold et al. would necessarily contain multiple exogenous nucleic acid sequences encoding a BAS1 polypeptide as a consequence of the methods by which they were transformed (direct gene transfer and *Agrobacterium*-mediated gene transfer). While Mangold et al. do not explicitly teach that their genetically modified plants have dwarf adult stature or comprise darker green leaves in adult plants, the genetically modified plants taught by Mangold et al. would necessarily have these characteristics since they are transformed with an exogenous nucleic acid sequence encoding a BAS1 polypeptide and express the encoded polypeptide (page 133 Figure 2). While Mangold et al. do not explicitly teach that their genetically modified plants produce transgenic seed, the genetically modified plants taught by Mangold et al. would necessarily produce transgenic seed, as tobacco and *Arabidopsis* are seed plants.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mangold et al. (Plant Science, Vol. 96, pages 129-136, 1994) in view of Persans et al. (Plant Physiology, 1995, Vol. 109, pages 1483-1490), and in further view of Lyznik et al. (The Plant Journal, 1995, Vol. 8, No. 2, pages 177-186).

The claims are drawn to a genetically modified monocotyledonous plant comprising at least one exogenous sequence encoding a BAS1 polypeptide in its genome wherein the plant is characterized as having dwarf adult stature, wherein the plant comprises darker green leaves in adult plants and wherein the exogenous nucleic acid sequence is operably associated with a regulatory sequence comprising an inducible promoter, and a seed.

The teachings of Mangold et al. are discussed above in the rejection under 35 USC 102.

Mangold et al. do not teach genetically modified monocotyledonous plants, or the use of an inducible promoter.

Persans et al. teach that plant cytochrome P450s are known to participate in the detoxification of the herbicides, including the detoxification of triasulfuron in the monocotyledonous plant maize (page 1483 abstract; page 1483 column 1 through page 1484 column 1). Persans et al. further teach that maize cytochrome P450s capable of binding and metabolizing triasulfuron are differentially induced by naphthalic anhydride and triasulfuron (page 1483 abstract; page 1488 column 2 through page 1489 column 2).

Lyznik et al. teach the use of a soybean heat-shock inducible promoter (Gmhsp 17.5E) to direct at will the expression of gus A and FLP genes in maize cells (page 177 abstract; page 178 Figure 1; page 179 Figure 2; page 180 Figures 4-6; page 181 Figures 7-8).

Given the success of Mangold et al. in cloning a plant sequence encoding a cytochrome P450 (CYP72 family) obtained from *Catharanthus roseus*, and given the teachings of Persans et al. that plant cytochrome P450s are known to participate in the detoxification of triasulfuron in the monocotyledonous plant maize, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to transform monocotyledonous maize plants with a sequence known to encode a plant cytochrome P450, such as the *Catharanthus roseus* sequence taught by Mangold et al. One of ordinary skill in the art would have been motivated to do so in order to test the effect of expressing the cytochrome P450 on triasulfuron tolerance. It also would have been obvious to express at will a sequence known to encode a plant cytochrome P450 using an inducible promoter, such as the soybean heat-shock inducible promoter Gmhsp 17.5E taught by Lyznik et al., which functions in both monocots (maize) and dicots (soybean). One of ordinary skill in the art would have been motivated to do so in order to control at will the expression of the transgene product relative to endogenous cytochrome P450s, which are induced only at specific times and under specific conditions.

Allowable Subject Matter

Claims 5, 6, 14, 16, 24 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Remarks

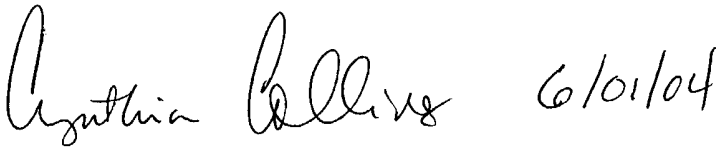
No claim is allowed.

Claims 1-11, 14, 16, 24 and 26 are deemed free of the prior art, due to the failure of the prior art to teach or suggest methods for producing a genetically modified plant characterized as having dwarf adult stature and exhibiting green foliage that is darker than a wild-type plant by transforming a plant with an exogenous nucleic acid sequence encoding a BAS 1 polypeptide of SEQ ID NO:2, or plants transformed therewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  6/01/04